

Listing of claims:

1-164. (Canceled)

165. (Currently amended) A method of activating a double-stranded RNA nuclease, comprising:

(i) contacting the nuclease with a double-stranded ~~RNA~~ nucleic acid comprising a first oligonucleotide and a second oligonucleotide, wherein:

at least one of said first and said second oligonucleotides comprises at least four consecutive 2'-hydroxyl ribonucleosides and at least one chemical modification;

said first and said second oligonucleotides are hybridized to each other; and

said first and said second oligonucleotides are not covalently linked to each other;

and

(ii) detecting activation of said double-stranded RNA nuclease.

166. (Canceled)

167. (Currently amended) The method of claim 165, wherein the at least one chemical ~~modifications increase~~ modification increases resistance of said oligonucleotide to single-stranded nucleases and/or ~~increase~~ increases the affinity of said oligonucleotide to the other oligonucleotide.

168. (Previously presented) The method of claim 167, wherein at least one modification is 2'-methoxy.

169. (Previously presented) The method of claim 167, wherein at least one modification is 2'-fluoro.

170. (Currently amended) The method of claim 167, wherein at least one modification is 2'-O-(methoxyethyl) 2'-O-methoxyethyl.

171. (Previously presented) The method of claim 167, wherein at least one modification is a phosphorothioate internucleoside linkage.

172. (Previously presented) The method of claim 165, wherein said first oligonucleotide and said second oligonucleotide each have at least four consecutive 2'-hydroxyl ribonucleosides.

173. (Previously presented) The method of claim 172, wherein the 2'-hydroxyl residues of said first and said second oligonucleotides have phosphodiester linkages.

174. (Previously presented) The method of claim 172, wherein the 2'-hydroxyl residues of said first and said second oligonucleotides have phosphorothioate linkages.

175. (Previously presented) The method of claim 172, wherein the 2'-hydroxyl residues of said first oligonucleotide have phosphodiester linkages and the 2'-hydroxyl residues of said second oligonucleotide have phosphorothioate linkages.

176. (Previously presented) The method of claim 172 or claim 175, wherein said first and said second oligonucleotides further comprise flanking residues 5' and 3' of the 2'-hydroxyl ribonucleosides, wherein said flanking residues have phosphorothioate linkages.

177. (Previously presented) The method of claim 176, wherein said flanking residues of at least one of said first and said second oligonucleotides further comprises 2'-methoxynucleosides.

178. (Previously presented) The method of claim 176, wherein said flanking residues of each of said first and said second oligonucleotides further comprise 2'-methoxynucleosides.

179. (Previously presented) The method of claim 165, wherein at least one of said first and said second oligonucleotides comprises at least eight consecutive 2'-hydroxyl ribonucleosides.

180. (Previously presented) The method of claim 179, wherein said first oligonucleotide and said second oligonucleotide each comprise at least eight consecutive 2'-hydroxyl ribonucleotides.

181. (Previously presented) The method of claim 165, wherein each of said first and said second oligonucleotides are about 17 to about 20 nucleoside subunits in length.

182. (Previously presented) The method of claim 181, wherein each of said first and said second oligonucleotides are 17 subunits in length.

183. (Previously presented) The method of claim 181, wherein each of said first and said second oligonucleotides are 20 subunits in length.

184-201. (Canceled)

202. (Currently amended) A method of activating a double-stranded RNA nuclease comprising contacting the nuclease with a double-stranded ~~RNA~~ nucleic acid comprising a first oligonucleotide and a second oligonucleotide, wherein:

said first and said second oligonucleotides are independently 15 to 25 nucleoside subunits in length;

said first and said second oligonucleotides are hybridized to each other;

said first and said second oligonucleotides are not covalently linked to each other;

and

at least one of said first and said second oligonucleotides comprises at least four consecutive 2'-hydroxyl ribonucleosides and at least one chemical modification.

203. (Previously presented) The method of claim 202 wherein at least one chemical modification increases resistance to single-stranded nucleases.

204. (Previously presented) The method of claim 202 wherein at least one chemical modification increases affinity of said first oligonucleotide to said second oligonucleotide.

205. (Currently amended) The method of claim 202 wherein at least one ~~at least one~~ chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

206. (Previously presented) The method of claim 202 wherein at least one chemical modification is a phosphorothioate internucleoside linkage.

207. (Previously presented) The method of claim 202 wherein at least one chemical modification is a 2'-substituted sugar modification.

208. (Previously presented) The method of claim 202 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

209. (Previously presented) The method of claim 202 wherein at least one chemical modification is a 2'-methoxy sugar modification.

210. (Previously presented) The method of claim 202 wherein at least one chemical modification is a 2'-fluoro sugar modification.

211. (Previously presented) The method of claim 202 wherein at least one chemical modification is a 2'-O-methoxyethyl sugar modification.

212. (Previously presented) The method of claim 202 wherein each of said first and said second oligonucleotides comprises at least four consecutive 2'-hydroxyl ribonucleosides.

213. (Previously presented) The method of claim 202 wherein each of said first and said second oligonucleotides comprises at least one chemical modification.

214. (Previously presented) The method of claim 202 wherein each of said first and said second oligonucleotides comprises at least four consecutive 2'-hydroxyl ribonucleosides and at least one chemical modification.

215. (Previously presented) The method of claim 202 wherein said first oligonucleotide and said second oligonucleotide comprise at least 17 contiguous nucleotides which are 100% complementary to each other.

216. (Previously presented) The method of claim 202 wherein said first oligonucleotide is 100% complementary to said second oligonucleotide.

217. (Previously presented) The method of claim 202 wherein said first oligonucleotide and said second oligonucleotide are independently 17 to 20 nucleoside subunits in length.

218. (Previously presented) The method of claim 202 further comprising detecting activation of said double-stranded RNA nuclease.

219. (Currently amended) A method of activating a double-stranded RNA nuclease comprising contacting the nuclease with a double-stranded RNA nucleic acid comprising a first oligonucleotide and a second oligonucleotide, wherein:

said first and said second oligonucleotides are independently 15 to 25 nucleoside subunits in length;

said first and said second oligonucleotides are hybridized to each other;

said first and said second oligonucleotides are not covalently linked to each other;

and

at least one of said first and said second oligonucleotides comprises a plurality of

nucleoside subunits with 2'-hydroxyl pentofuranosyl sugar moieties; and at least one chemical modification.

220. (Previously presented) The method of claim 219 wherein at least one chemical modification increases resistance to single-stranded nucleases.

221. (Previously presented) The method of claim 219 wherein at least one chemical modification increases affinity of said first oligonucleotide to said second oligonucleotide.

222. (Previously presented) The method of claim 219 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

223. (Previously presented) The method of claim 219 wherein at least one chemical modification is a phosphorothioate internucleoside linkage.

224. (Previously presented) The method of claim 219 wherein at least one chemical modification is a 2'-substituted sugar modification.

225. (Previously presented) The method of claim 219 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

226. (Previously presented) The method of claim 219 wherein at least one chemical modification is a 2'-methoxy sugar modification.

227. (Previously presented) The method of claim 219 wherein at least one chemical modification is a 2'-fluoro sugar modification.

228. (Previously presented) The method of claim 219 wherein at least one chemical modification is a 2'-O-methoxyethyl sugar modification.

229. (Previously presented) The method of claim 219 wherein each of said first and said second oligonucleotides comprises a plurality of nucleoside subunits with 2'-hydroxyl pentofuranosyl sugar moieties.

230. (Previously presented) The method of claim 219 wherein each of said first and said second oligonucleotides comprises at least one chemical modification.

231. (Previously presented) The method of claim 219 wherein each of said first and

said second oligonucleotides comprises a plurality of nucleoside subunits with 2'-hydroxyl pentofuranosyl sugar moieties and at least one chemical modification.

232. (Previously presented) The method of claim 219 wherein said first oligonucleotide and said second oligonucleotide comprise at least 17 contiguous nucleotides which are 100% complementary to each other.

233. (Previously presented) The method of claim 219 wherein said first oligonucleotide is 100% complementary to said second oligonucleotide.

234. (Previously presented) The method of claim 219 wherein said first oligonucleotide and said second oligonucleotide are independently 17 to 20 nucleoside subunits in length.

235. (Previously presented) The method of claim 219 further comprising detecting activation of said double-stranded RNA nuclease.

236. (Currently amended) A method of activating a double-stranded RNA nuclease comprising contacting the nuclease with a double-stranded ~~RNA~~ nucleic acid comprising a first oligonucleotide and a second oligonucleotide, wherein:

said first and said second oligonucleotides are hybridized to each other;

said first and said second oligonucleotides are not covalently linked to each other;

and

each of said first and said second oligonucleotides comprises at least four consecutive 2'-hydroxyl ribonucleosides and at least one chemical modification.

237. (Previously presented) The method of claim 236 wherein at least one chemical modification increases resistance to single-stranded nucleases.

238. (Previously presented) The method of claim 236 wherein at least one chemical modification increases affinity of said first oligonucleotide to said second oligonucleotide.

239. (Previously presented) The method of claim 236 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

240. (Previously presented) The method of claim 236 wherein at least one chemical

modification is a phosphorothioate internucleoside linkage.

241. (Previously presented) The method of claim 236 wherein at least one chemical modification is a 2'-substituted sugar modification.

242. (Previously presented) The method of claim 236 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

243. (Previously presented) The method of claim 236 wherein at least one chemical modification is a 2'-methoxy sugar modification.

244. (Previously presented) The method of claim 236 wherein at least one chemical modification is a 2'-fluoro sugar modification.

245. (Previously presented) The method of claim 236 wherein at least one chemical modification is a 2'-O-methoxyethyl sugar modification.

246. (Previously presented) The method of claim 236 further comprising detecting activation of said double-stranded RNA nuclease.

247. (Currently amended) A method of activating a double-stranded RNA nuclease comprising contacting the nuclease with a double-stranded ~~RNA~~ nucleic acid comprising a first oligonucleotide and a second oligonucleotide, wherein:

said first and said second oligonucleotides are hybridized to each other;

said first and said second oligonucleotides are not covalently linked to each other;

said first and said second oligonucleotides are 100% complementary to each other; and

at least one of said first and said second oligonucleotides comprises at least four consecutive 2'-hydroxyl ribonucleosides and at least one chemical modification.

248. (Previously presented) The method of claim 247 wherein at least one chemical modification increases resistance to single-stranded nucleases.

249. (Previously presented) The method of claim 247 wherein at least one chemical modification increases affinity of said first oligonucleotide to said second oligonucleotide.

250. (Previously presented) The method of claim 247 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified

nucleobase.

251. (Previously presented) The method of claim 247 wherein at least one chemical modification is a phosphorothioate internucleoside linkage.

252. (Previously presented) The method of claim 247 wherein at least one chemical modification is a 2'-substituted sugar modification.

253. (Previously presented) The method of claim 247 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

254. (Previously presented) The method of claim 247 wherein at least one chemical modification is a 2'-methoxy sugar modification.

255. (Previously presented) The method of claim 247 wherein at least one chemical modification is a 2'-fluoro sugar modification.

256. (Previously presented) The method of claim 247 wherein at least one chemical modification is a 2'-O-methoxyethyl sugar modification.

257. (Previously presented) The method of claim 247 further comprising detecting activation of said double-stranded RNA nuclease.

258. (New) The method of claim 219, wherein the double-stranded RNA nuclease is not in a cell.